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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,612	01/26/2006	Gianfranco Gilardi	Q88296	4772
23373 7590 08/06/2008 SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037				
EXAMINER MEAH, MOHAMMAD Y				
ART UNIT		PAPER NUMBER		
1652				
MAIL DATE		DELIVERY MODE		
08/06/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/537,612

Applicant(s)

GILARDI, GIANFRANCO

Examiner

MD. YOUNUS MEAH

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18, 20-23, 26 and 27 is/are pending in the application.
- 4a) Of the above claim(s) 6-1116-18, 20, 23, 26-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 15, 21-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/888)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

In response to a previous Office action (mailed on 12/31/2007), Applicants filed a response and amendment is received on April 28, 2008. Claims 1-18, 20-23, 26-27 are pending. Claims 6-11, 16-18, 20, 23, 26-27 remain withdrawn. Claims 1 and 14 are amended.

Applicants' arguments filed on April 4, 2008, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections**35 U.S.C 112**

35 U.S.C. 112 1st paragraph *written description*

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Rejection of claims 1-5, 15, 21-22 under 35 U.S.C. 112, 35 USC first

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paragraphs written description is withdrawn after amendments of the claims.

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35 U.S.C. 112 1st paragraph Enablement

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 15, 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the protein of SEQ ID NO: 11 comprising heme redox center does not reasonably provide enablement for a protein of 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 and any redox center comprising any metal atom which is stable at different oxidation states. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-5, 15, 21-22 are so broad as to encompass a protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 and any redox center comprising any metal atom which is stable at different oxidation states. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of redox centers broadly encompassed by the claims. Specification teaches at page 2, a redox center comprising a moiety that

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capable of accepting and donating electron, such moiety comprise FMN, FAD or haem, etc. However protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 has been shown in the specification to have a structure suitable for binding only to a haem redox center (which binds only to Fe atoms). Other redox centers have different structures and thus would require different amino acids within the 4 α -helices to be bound. However, the claim is limited to the 4 α -helices of SEQ ID NO:11 and a skilled artisan would NOT expect protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 to bind other redox centers (binding to other metal atoms).

In view of the great breath of the claims, amount of experimentation required to isolate polypeptide molecule having specific redox activity from these enormous number of polypeptide molecules and , the lack of guidance, working examples, unpredictability of the art in predicting the function (redox activity) from protein's structure (Whisstock, et al. Quarterly Rev. Biophy. 2003, 36, pp 307-340), the claimed invention would require undue experimentation. As such the specification fails to teach one of ordinary skill how to use the full scope of the claims.

The specification does not support the broad scope of the claims which encompass a protein of 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11, and any redox center comprising any metal atom because the specification does not establish: (A) regions of the protein structure having haem redox center which may be modified to bind other metal atoms without effecting redox activity; (B) the general tolerance of haem redox center to modification and extent of such tolerance; (C)

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a rational and predictable scheme for modifying ~~haem redox center~~ residues with an expectation of obtaining the desired biological function, ~~(D) any other redox center which SEQ ID NO:11 is capable of binding;~~ and ~~(E)~~ the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

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Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 and any redox center comprising any metal atom which is stable at different oxidation states. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of ROP activity, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

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Applicants contend that claims 1-5, 15, 21-22 meet the enablement requirement of § 112, first paragraph. Applicant argue that amended claim comprises a protein having a redox center that bind a metal atom which is stable at different oxidation states is enabled because specification teach ROP (repressor of primer) comprising SEQ ID NO: 11 bind haem moiety by axial co-ordination. As would be appreciated by the skilled artisan, the distinctive feature of a haem molecule that permits this geometry

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is the equatorial planar porphyrin ring which leaves the axial co-ordination positions of the iron atom available to interact with the ligands of the residues introduced into the helix. As shown in Figure 1B of Applicants' disclosure, the structure of the 4- α -helix bundle motif formed from the α -helices of the ROP (repressor of primer) of SEQ ID NO: 11 enables it to co-ordinate the metal atom in the opposed orientation of the ligands of these residues in the helices. They further argue that using the molecular modeling approach and experimental assays described in Applicants' disclosure, one of skill in the art would readily understand which metal atoms, or molecules comprising metal atoms having redox properties, could be utilized in the present invention, without embarking on undue experimentation.

It is not found persuasive because as discussed above the scope of redox center claimed in these claims is broadly include any protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 and any redox center which bind any metal atom which is stable at different oxidation states. Specification defines at page 2 a redox center comprising a moiety that capable of accepting and donating electron, such moiety comprise FMN, FAD or haem, etc. However protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 has been shown to be capable of binding only to a haem redox center. Other redox centers have different structures and thus would require different amino acids within the 4 α -helices to be bound. However, the claim is limited to the 4 α -helices of SEQ ID NO:11 and a skilled artisan would NOT expect a protein comprising 4 α -helices of ROP (repressor of

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primer) comprising SEQ ID NO: 11 to bind other redox centers (binding to other metal atoms).

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mohammad Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you

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Deleted: The redox center comprise in these claim comprise any structure. As the structure of the claimed redox center that recite in the instant claims are not defined in any way, one of ordinary skill in the art would not be able to make and use any protein comprising 4 α -helices of ROP (repressor of primer) comprising SEQ ID NO: 11 and said redox center and require undue experimentation to find out which of these proteins with said redox centers bind which metal.

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have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mohammad Younus Meah, PhD

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